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| (51) International Patent Classification 6:<br><b>C12N 15/49, A61K 31/70, 48/00</b>   |  | A3   | (11) International Publication Number: <b>WO 97/31115</b><br><br>(43) International Publication Date: <b>28 August 1997 (28.08.97)</b> |
| <br>(21) International Application Number: <b>PCT/US97/02294</b><br><br>(22) International Filing Date: <b>18 February 1997 (18.02.97)</b><br><br>(30) Priority Data:<br>60/012,082 22 February 1996 (22.02.96) US<br>9607293.9 9 April 1996 (09.04.96) GB  |  | <br>(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). |  |
| <br>(71) Applicant ( <i>for all designated States except US</i> ): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).<br><br>(72) Inventors; and<br><br>(75) Inventors/Applicants ( <i>for US only</i> ): SHIVER, John, W. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). DAVIES, Mary-Ellen [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). FREED, Daniel, C. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). LIU, Margaret, A. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). PERRY, Helen, C. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).<br><br>(74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). |  | <br>Published<br><i>With international search report.</i><br><i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i><br><br>(88) Date of publication of the international search report:<br><b>9 October 1997 (09.10.97)</b>   |  |
| <br>(54) Title: <b>SYNTHETIC HIV GENES</b><br><br>(57) Abstract<br><br>Synthetic DNA molecules encoding HIV genes and modifications of HIV genes are provided. The codons of the synthetic molecules use codons preferred by the projected host cell. The synthetic molecules may be used as a polynucleotide vaccine which provides effective immunoprophylaxis against HIV infection through neutralizing antibody and cell-mediated immunity.  |  |  |  |

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 97/02294

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 6 C12N15/49 A61K48/00 A61K31/70

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 C12N A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| X          | WO 95 20660 A (UNIVERSITY OF MASSACHUSETTS MEDICAL CENTER) 3 August 1995<br>see page 45, line 16 - page 62, line 10<br>---  | 1-5,7,9               |
| X          | AIDS RESEARCH AND HUMAN RETROVIRUSES,<br>vol. 11, no. 8, August 1995,<br>pages 933-943, XP002036839<br>K. OKUDA ET AL.: "Induction of potent humoral and cell-mediated immune responses following direct injection of DNA encoding the HIV type 1 env and rev gene products"<br>see the whole document<br>--- | 1-5,7,9<br>-/-        |

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

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- \*E\* earlier document but published on or after the international filing date
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- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*&\* document member of the same patent family

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|---|--|
| Date of the actual completion of the international search   | Date of mailing of the international search report |
| 5 August 1997   | 21.08.97   |
| Name and mailing address of the ISA<br>European Patent Office, P.B. 5818 Patentaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+ 31-70) 340-3016 | Authorized officer<br><br>Cupido, M                |

## INTERNATIONAL SEARCH REPORT

Internat'l Application No  
PCT/US 97/02294

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT |  |         |
|--|--|---------|
| Category   | Relevant to claim No.  |         |
| X  | PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,<br>vol. 90, 1 May 1993, WASHINGTON US,<br>pages 4156-4160, XP000608482<br>B. WANG ET AL.: "Gene inoculation generates immune responses against human immunodeficiency virus type 1"<br>see the whole document<br>--- | 1-5,7,9 |
| X  | WO 94 16737 A (D.B. WEINER ET AL.) 4<br>August 1994<br>see page 59, line 26 - page 89, line 22<br>---  | 1-5,7,9 |
| P,X  | WO 96 21356 A (VANDERBILT UNIVERSITY) 18<br>July 1996<br>see the whole document<br>---   | 1-5,7,9 |
| P,X  | DATABASE WPI<br>Section Ch, Week 9641<br>Derwent Publications Ltd., London, GB;<br>Class B04, AN 96-408330<br>XP002036840<br>& JP 08 198 774 A (OKUDA K) , 6 August<br>1996<br>see abstract<br>-----   | 1-5,7,9 |

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 97/02294

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 4-6, 8, 9

because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 4-6, 8 and 9 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.

2.  Claims Nos.:

because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3.  Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

|                 |                         |
|-----------------|-------------------------|
| Interr          | national Application No |
| PCT/US 97/02294 |                         |

| Patent document cited in search report | Publication date | Patent family member(s)   | Publication date   |
|--|------------------|---|--|
| WO 9520660 A                           | 03-08-95         | CA 2181832 A<br>EP 0740704 A<br>US 5620896 A  | 03-08-95<br>06-11-96<br>15-04-97   |
| WO 9416737 A                           | 04-08-94         | US 5593972 A<br>AU 675702 B<br>AU 6232094 A<br>EP 0681483 A<br>HU 73099 A<br>JP 8509694 T<br>ZA 9400493 A | 14-01-97<br>13-02-97<br>15-08-94<br>15-11-95<br>28-06-96<br>15-10-96<br>03-01-95 |
| WO 9621356 A                           | 18-07-96         | AU 2958795 A  | 31-07-96   |